

Synthesis of H-TAP-Boc molecule

Synthesis of Cbz-TAP

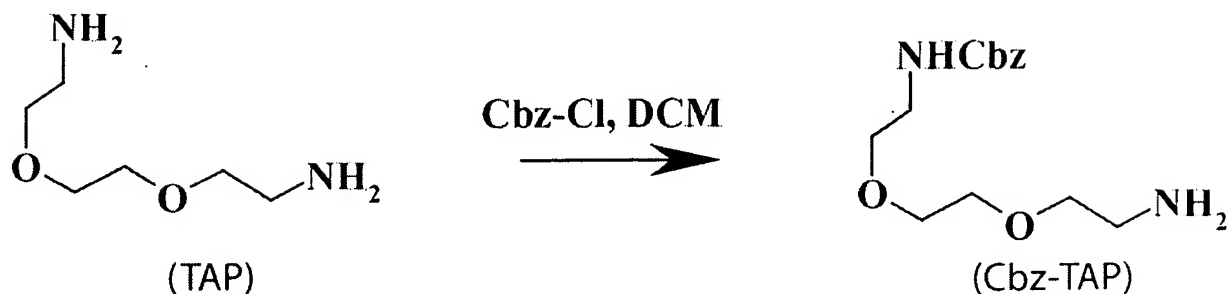


FIG. 1A

Synthesis of Cbz-TAP-Boc

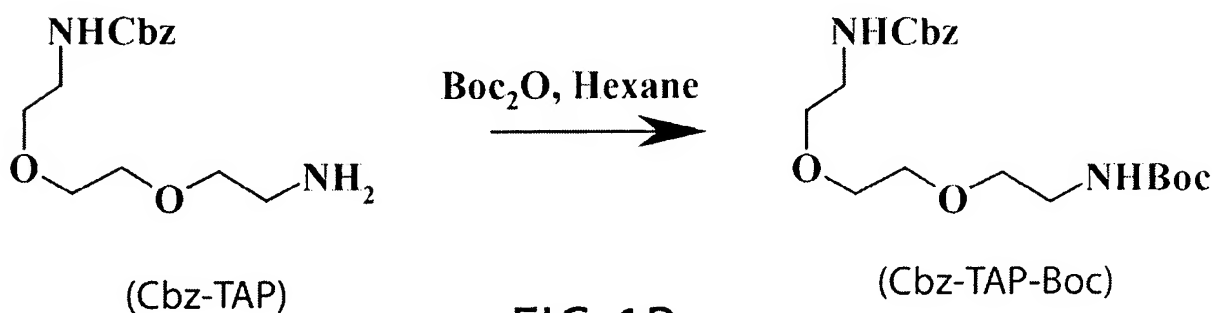


FIG. 1B

Synthesis of Boc-TAP

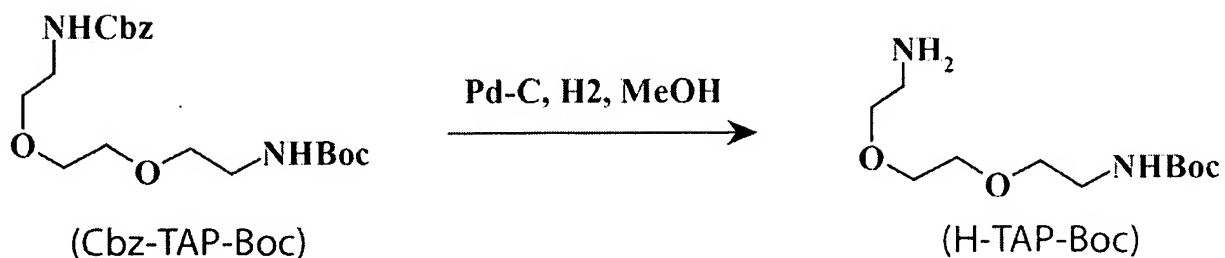


FIG. 1C

Attaching Spacer to Peptide with C-Terminus

Peptide with free C-terminus:

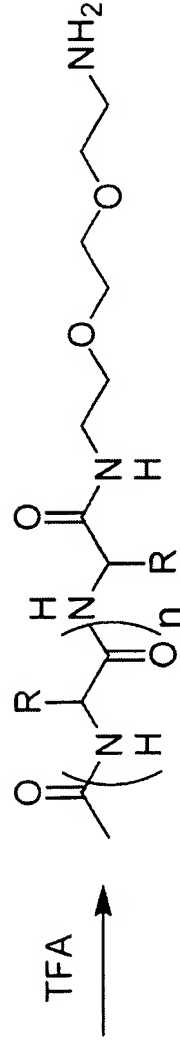
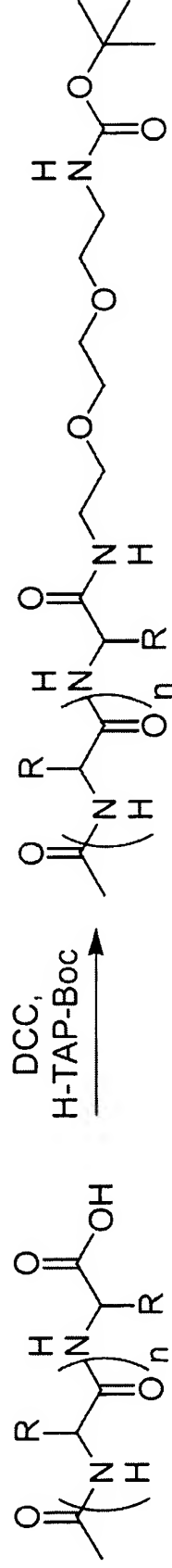


FIG. 2

Attaching Spacer to Peptide with Free Side-Chain Acid

Peptide with free side-chain acid:

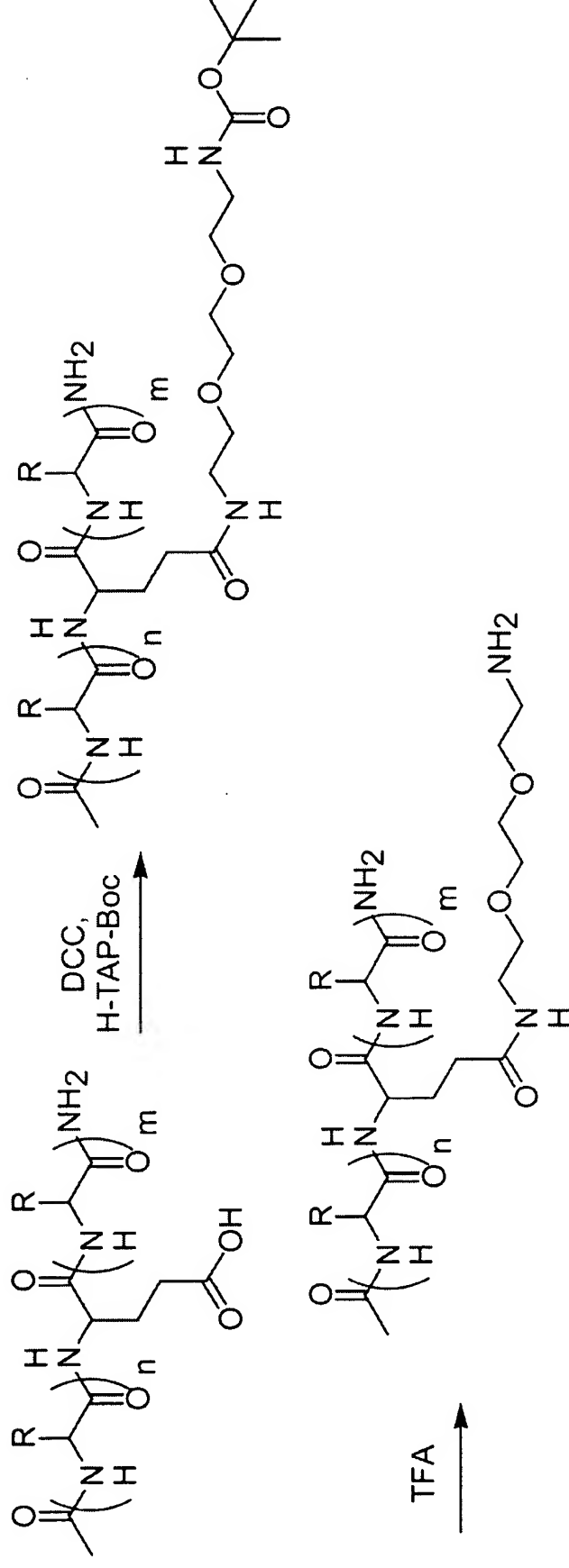


FIG. 3

PEGylation of Peptide, with mPEG-NPC

Peptide with TAP on C-terminus:

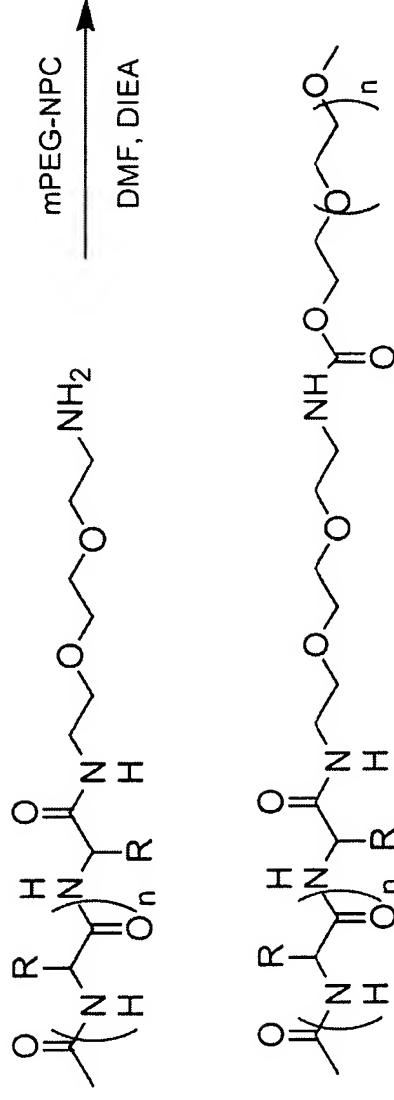


FIG. 4A

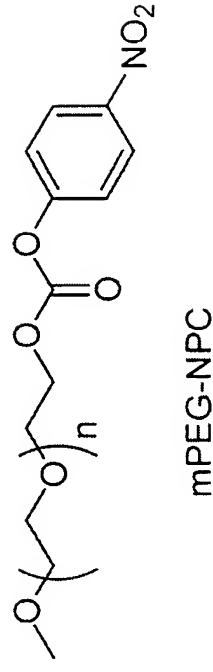


FIG. 4B

PEGylation of Peptide, with mPEG-SPA

Peptide with TAP on C-terminus:

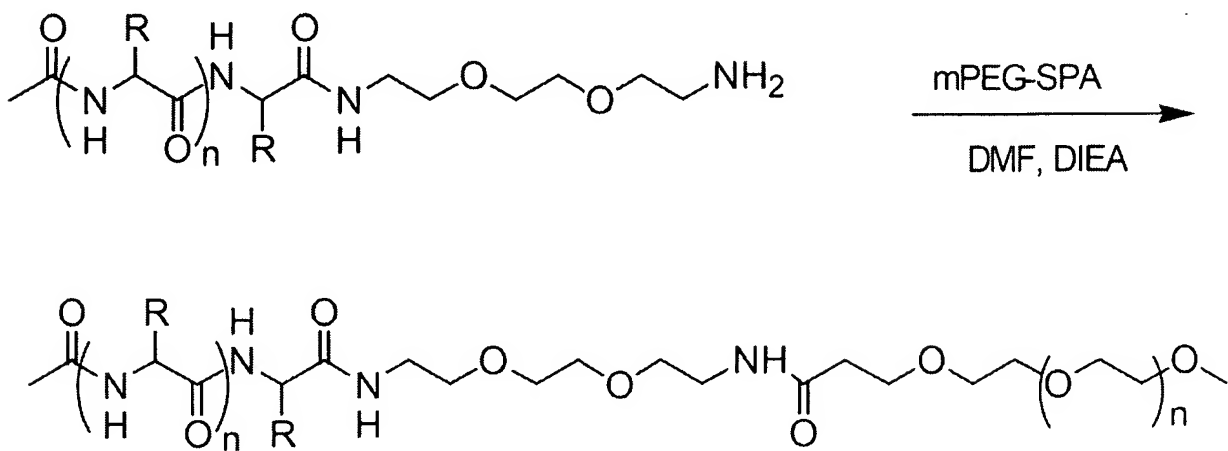
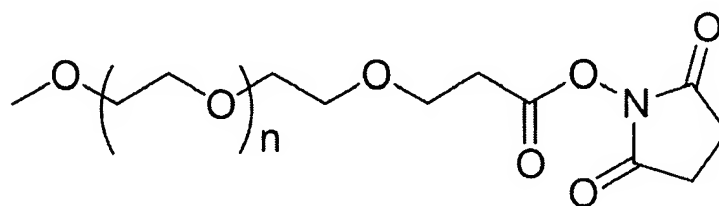


FIG. 5A



mPEG-SPA

FIG. 5B

Attaching Spacer and Synthesizing Peptide

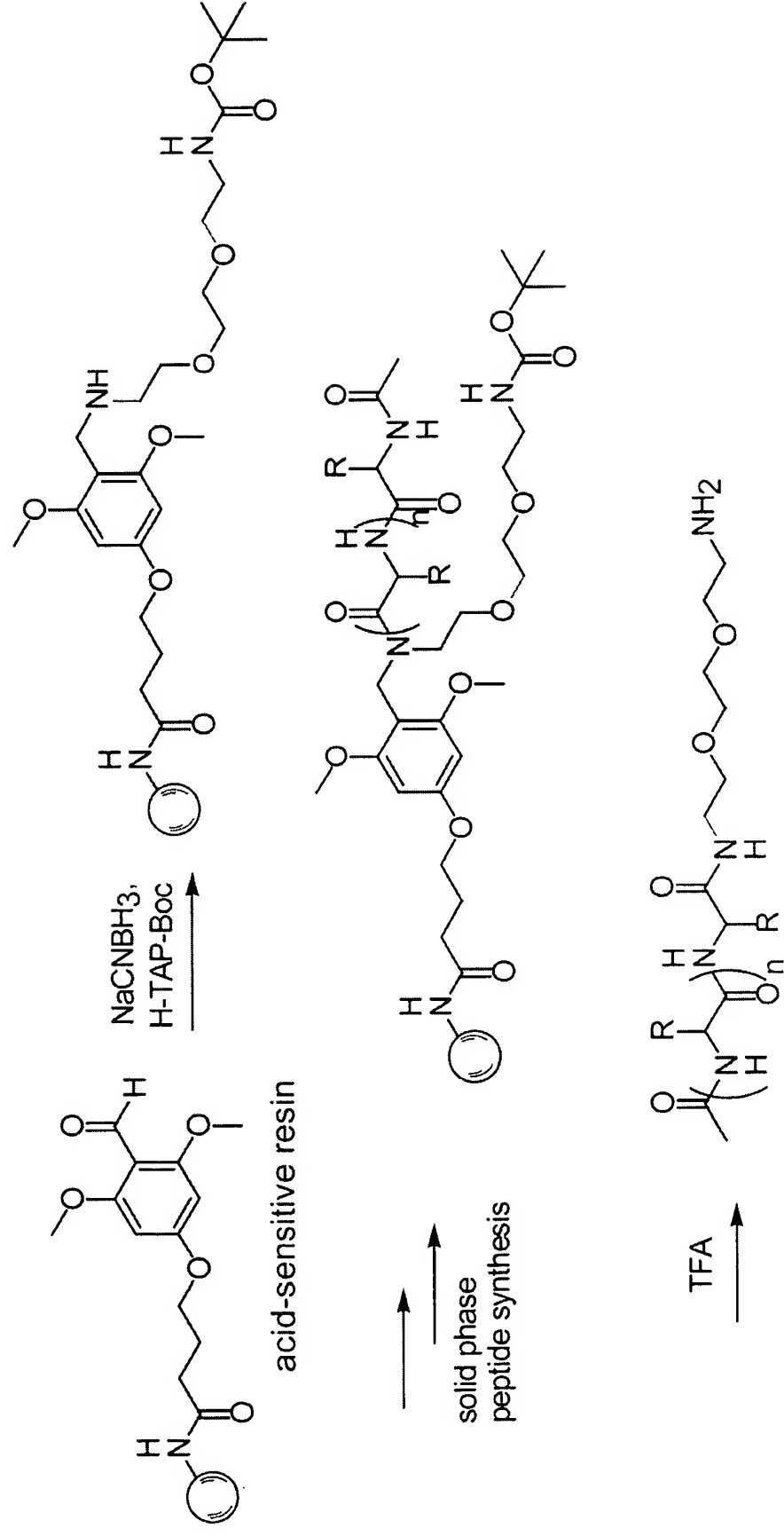


FIG. 6

Synthesis of Peptide Dimer with Spacer, Attached to Resin

Synthesis of TentaGel-Linker:

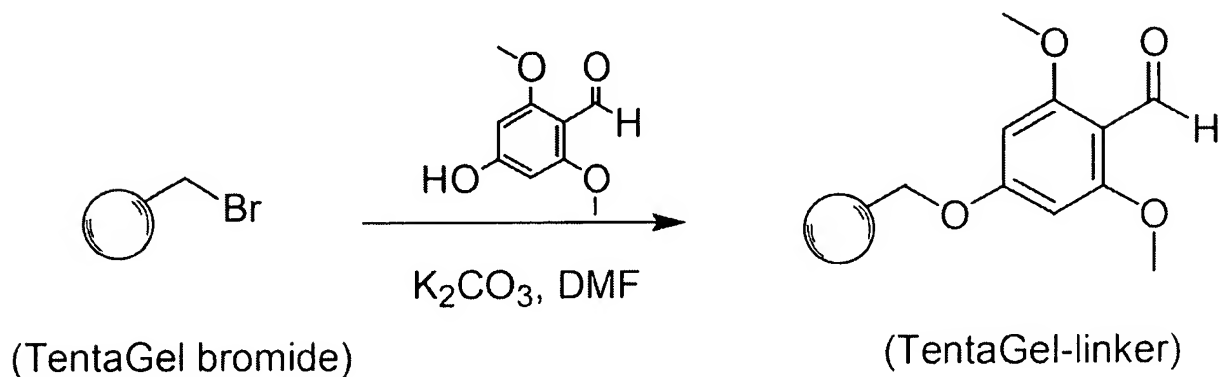


FIG. 7A

Synthesis of TentaGel-Linker-TAP(Boc)

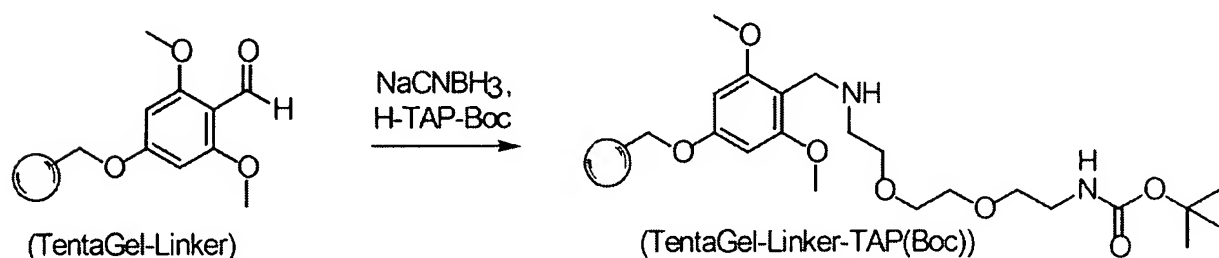


FIG. 7B

Synthesis of TentaGel-Linker-TAP-Lys

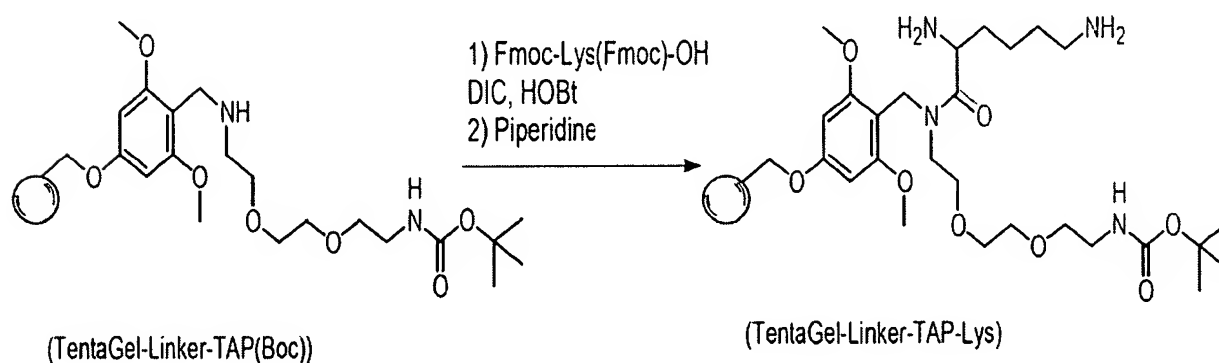


FIG. 7C

Chemical reaction scheme showing the solid phase peptide synthesis of a complex peptide. The starting material is a resin-bound intermediate with a 3,4,5-trimethoxyphenyl group, a tert-butyl ester, and a primary amine. The reaction proceeds via solid phase peptide synthesis to form the final product, which has an additional peptide chain attached to the amine.

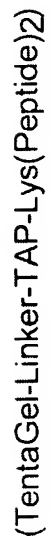


FIG. 7D

Cleavage from Resin

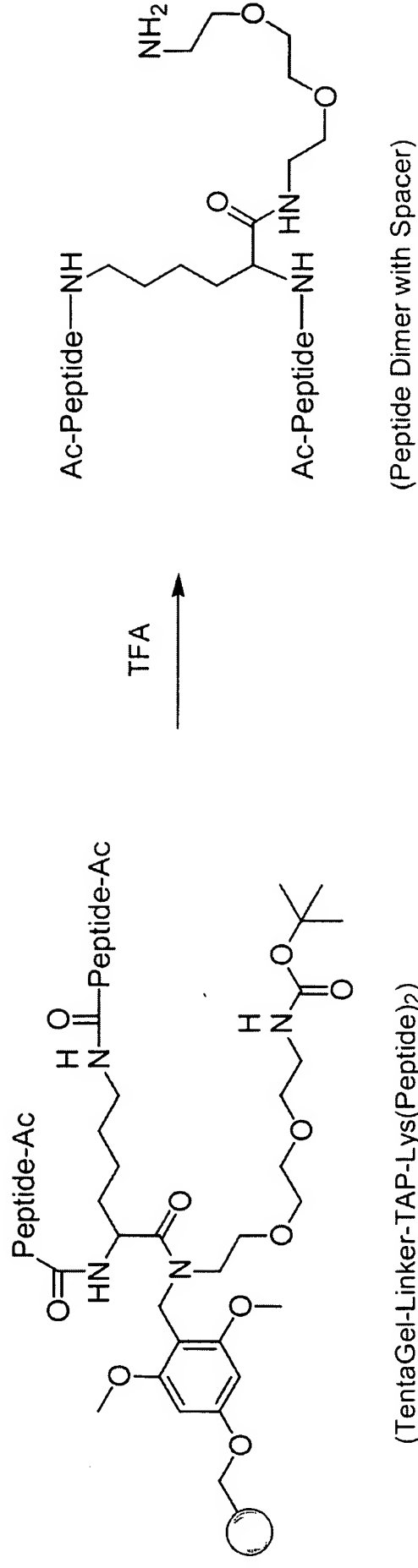
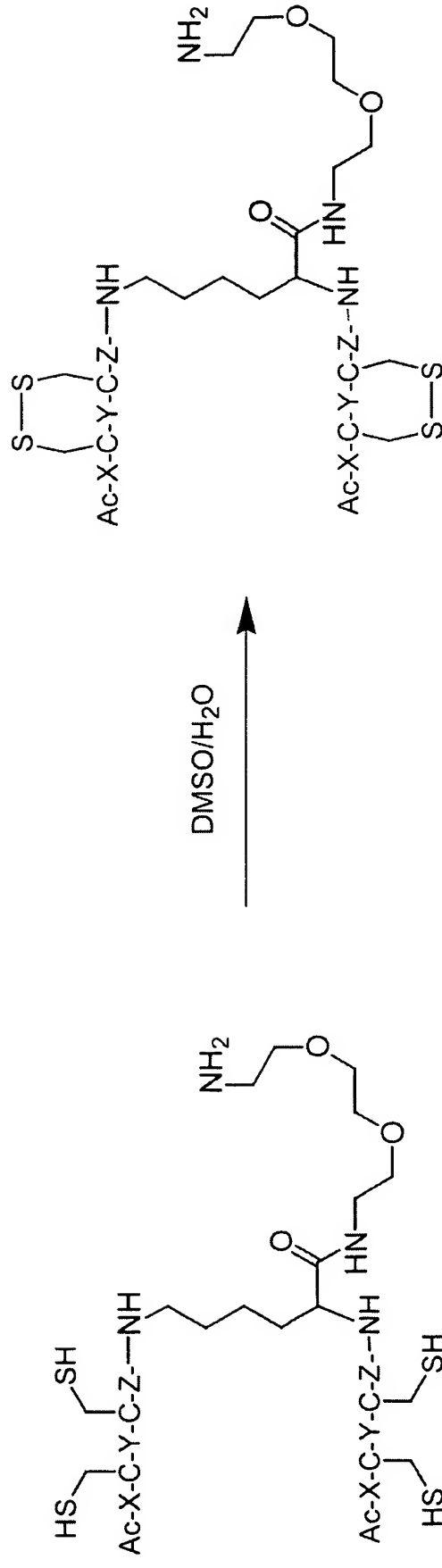


FIG. 7E

Oxidation



Dimeric peptide (XYZ) containing reduced cysteine residues

Dimeric peptide (XYZ) containing oxidized disulfide bonds

FIG. 7F

PEGylation of Peptide Dimer with Spacer, with mPEG-NPC

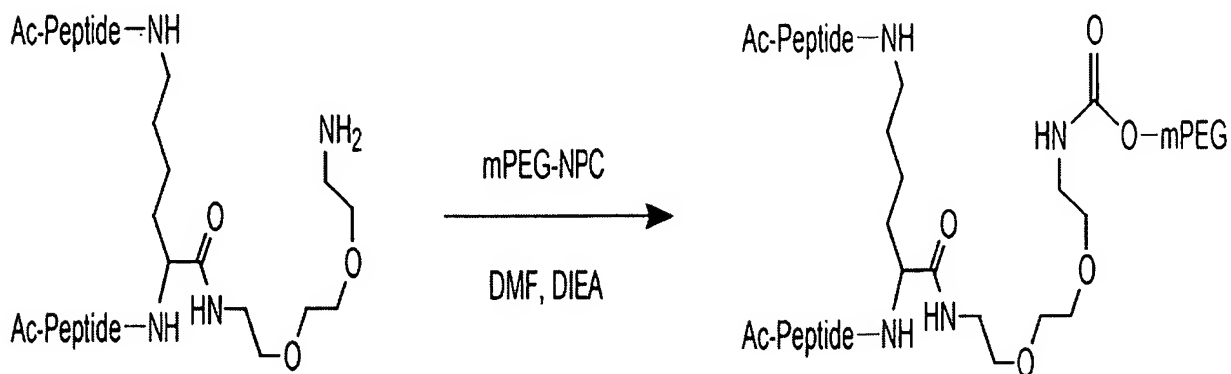


FIG. 8A

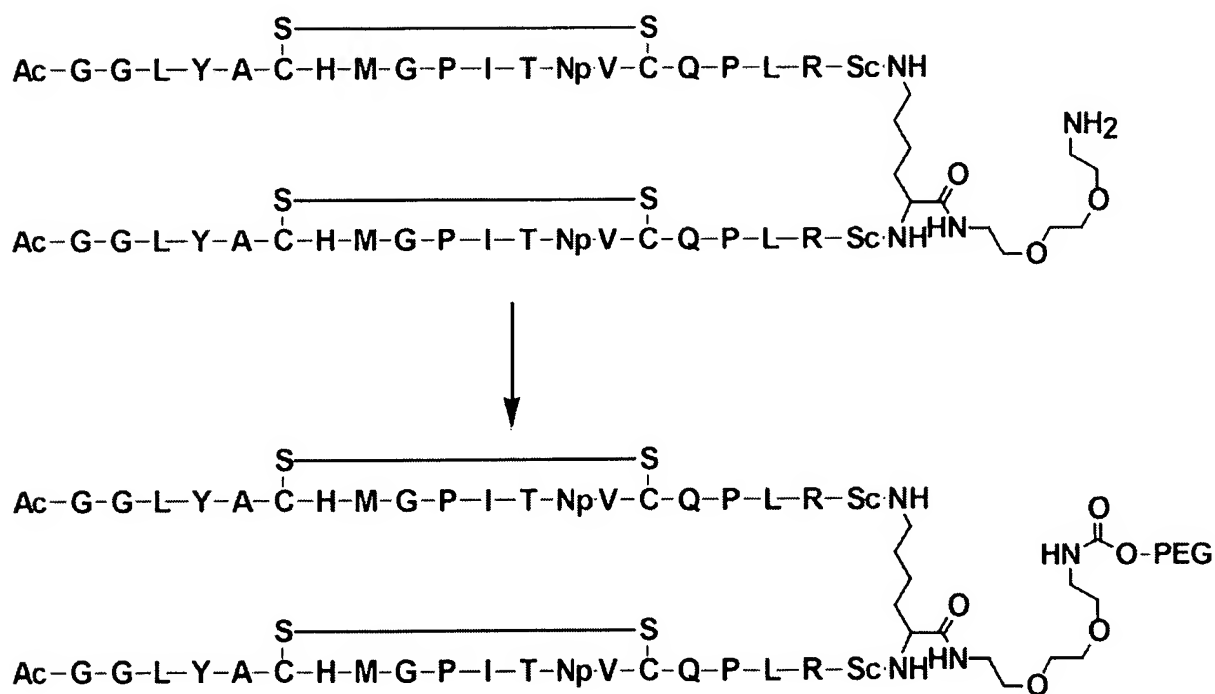
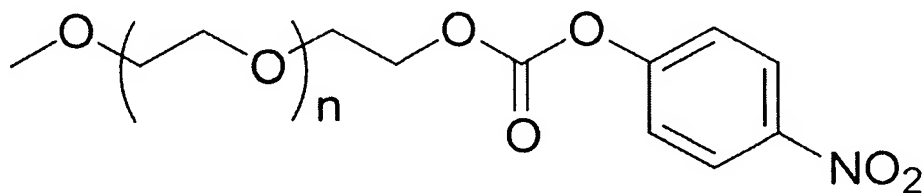


FIG. 8B



mPEG-NPC

FIG. 8C

PEGylation of Peptide Dimer with Spacer, with mPEG-SPA

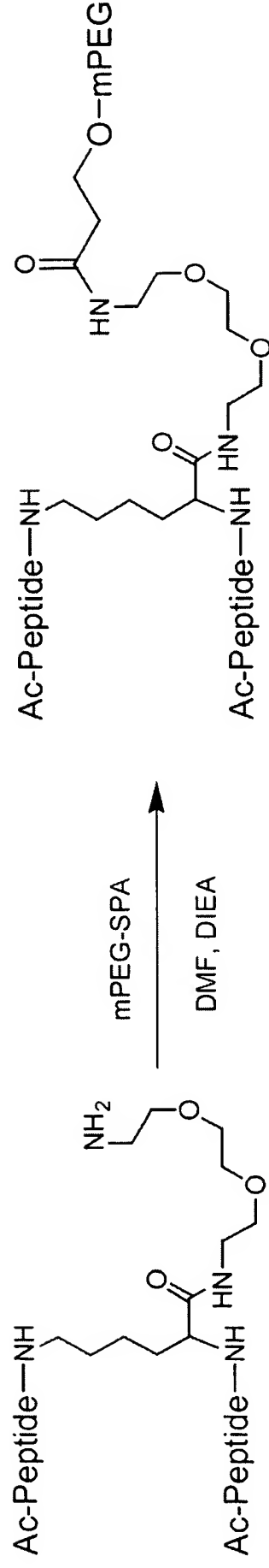
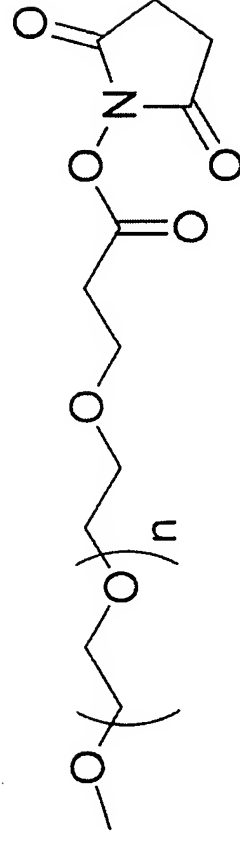


FIG. 9A



mPEG-SPA

FIG. 9B

Ion Exchange Purification

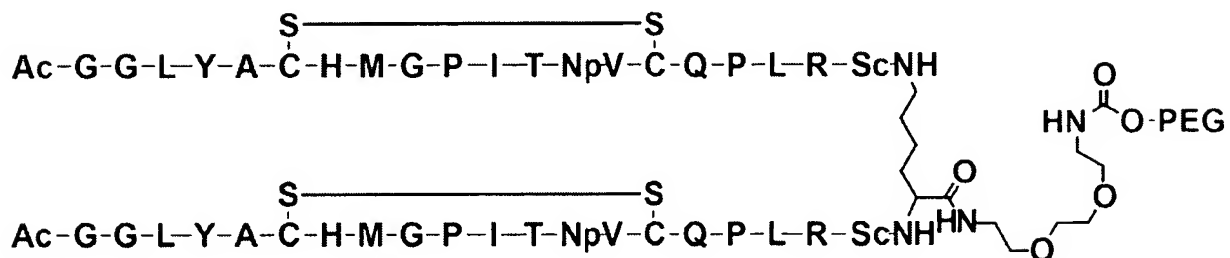
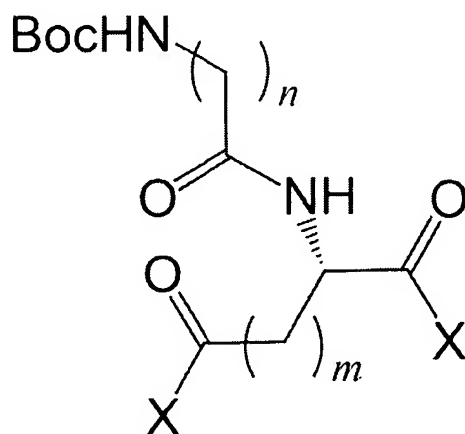


FIG. 10



$m=1-5$, $n = 1-14$, m and n are integers

FIG. 11A

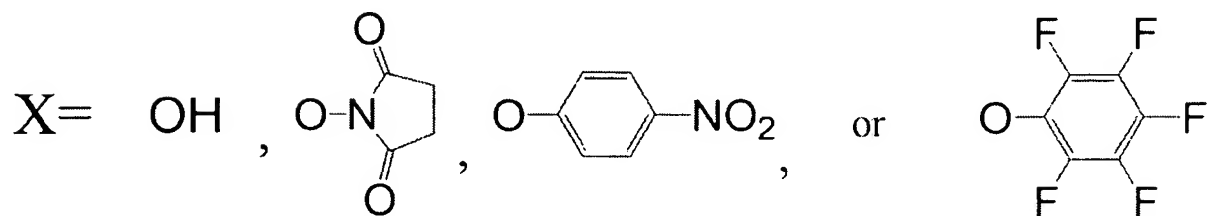
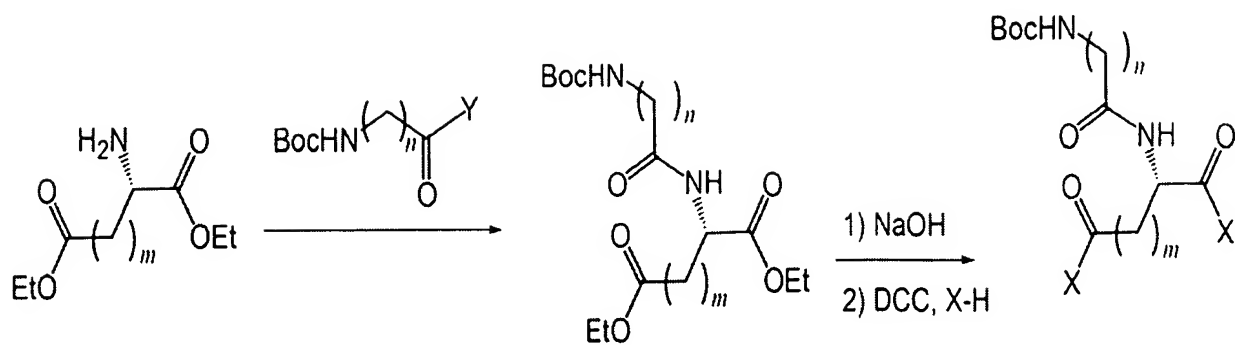
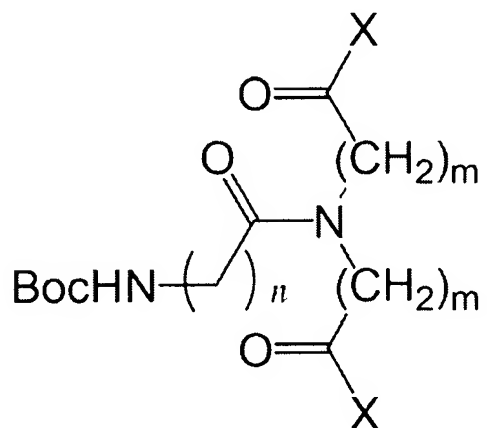


FIG. 11B



$m=1-5$, $n = 1-14$, m and n are integers

FIG. 11C



$m=1-5$, $n = 1-14$, m and n are integers

FIG. 12A

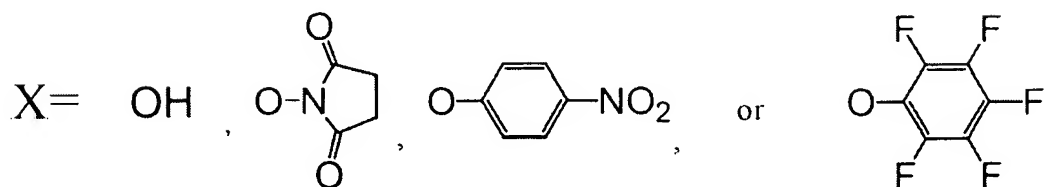
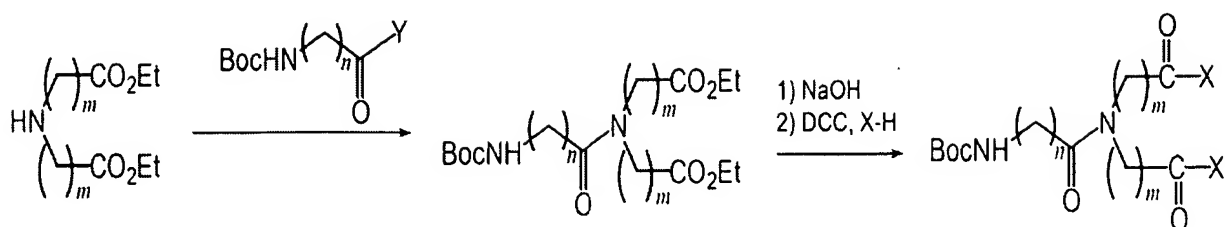


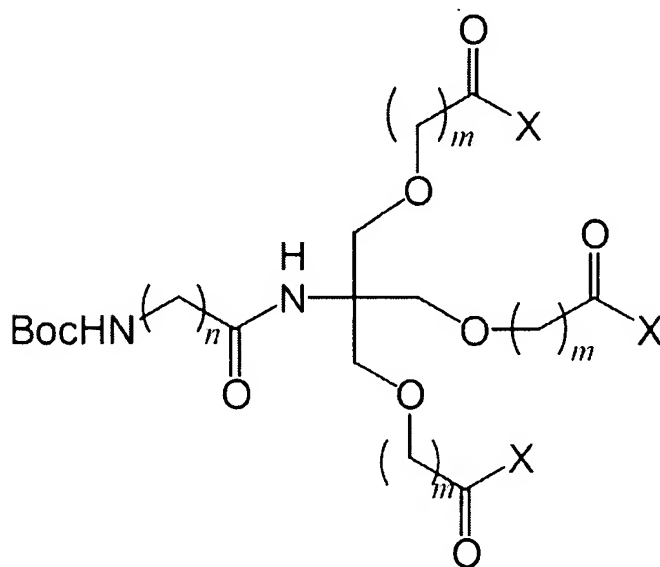
FIG. 12B



$m=1-5$, $n = 1-14$, m and n are integers

FIG. 12C

Synthesis of Homotrifunctional Molecules
Branched homotrifunctional molecules having the structure



$m=1-2$, $n = 1-6$, m and n are integers

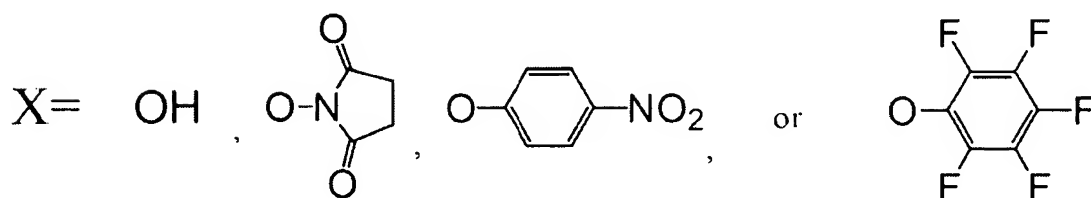
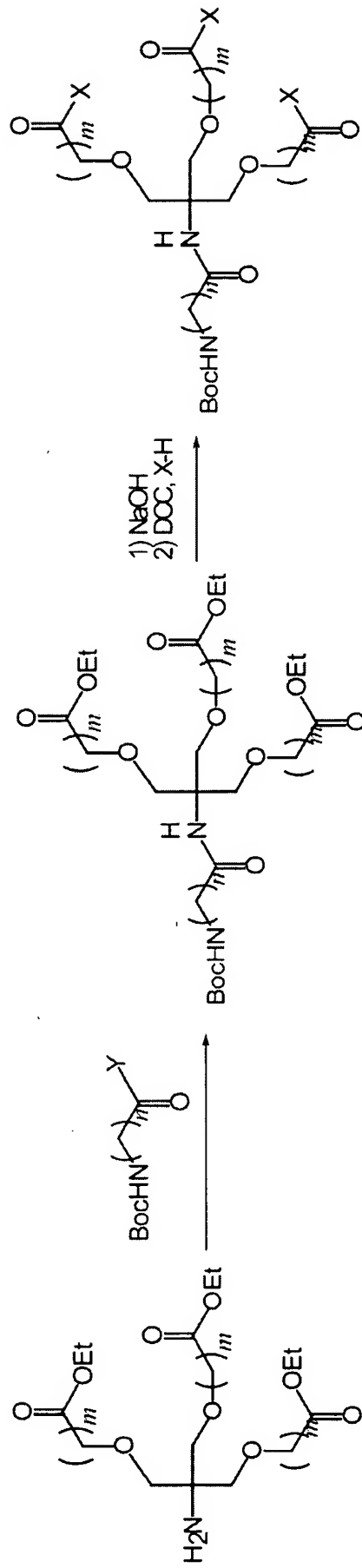


FIG. 13A



$m=1-2, n=1-6, m \text{ and } n \text{ are integers}$

FIG. 13B

C-Terminus Dimerization and PEGylation Using A Trifunctional Molecule

A trifunctional molecule having the structure

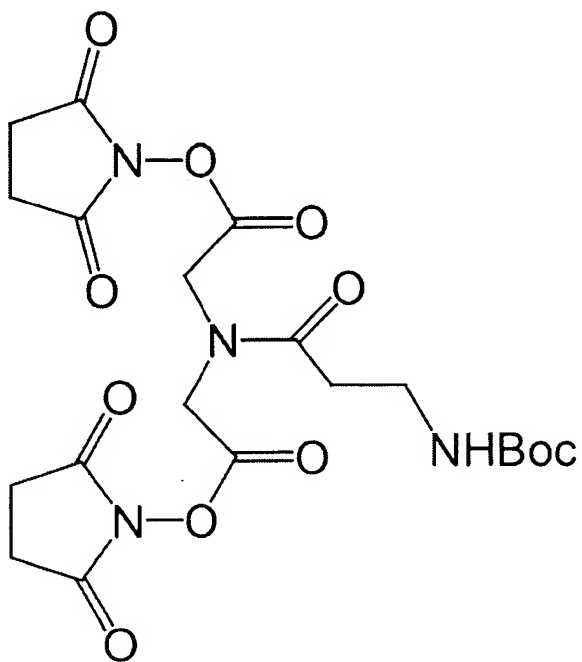
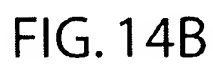


FIG. 14A



N-Terminus Dimerization and PEGylation Using A Trifunctional Molecule

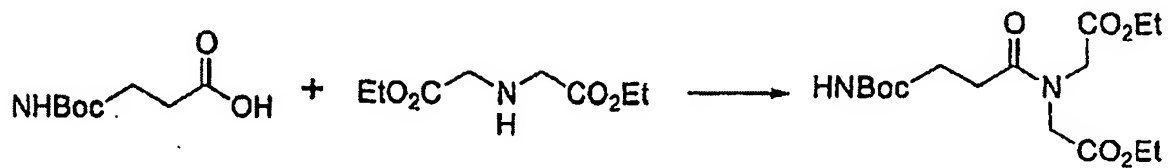


FIG. 15A

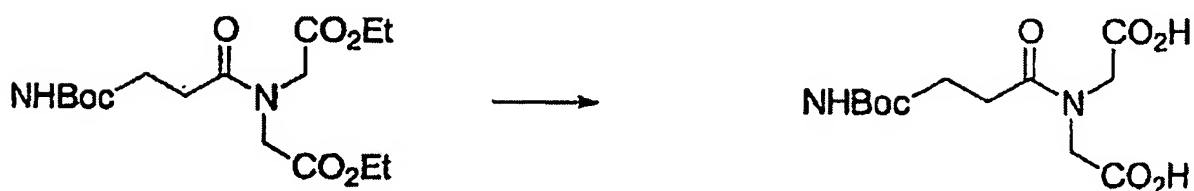


FIG. 15B

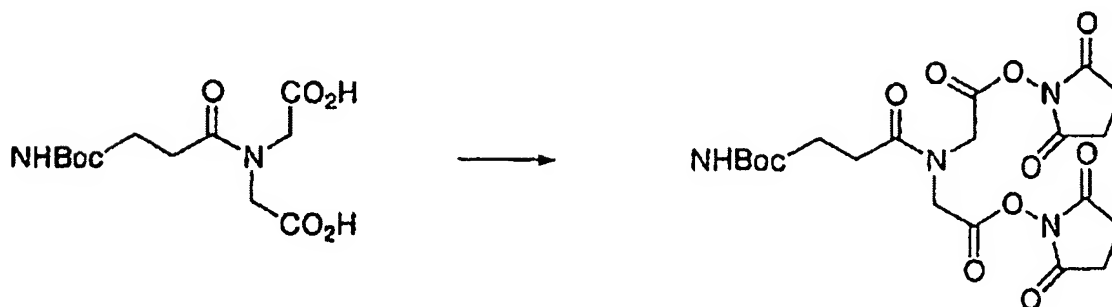


FIG. 15C

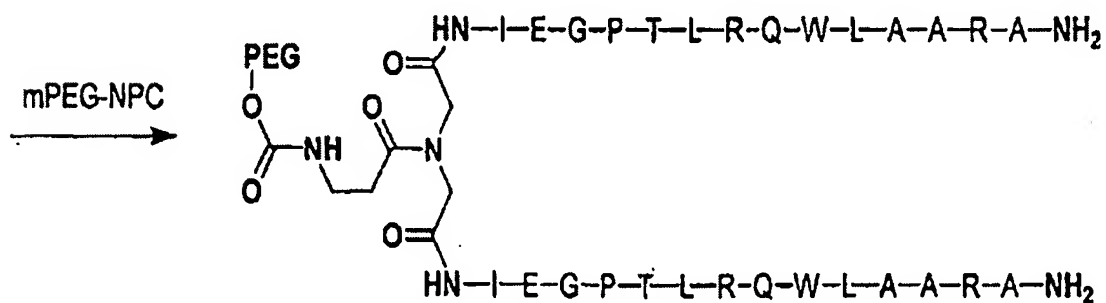
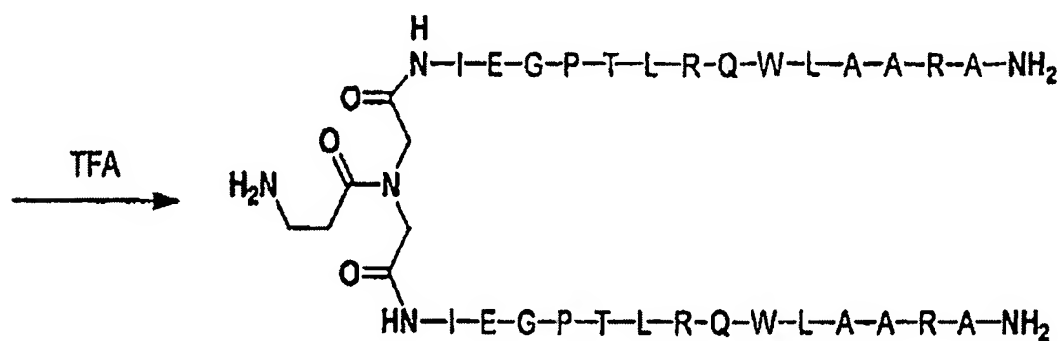
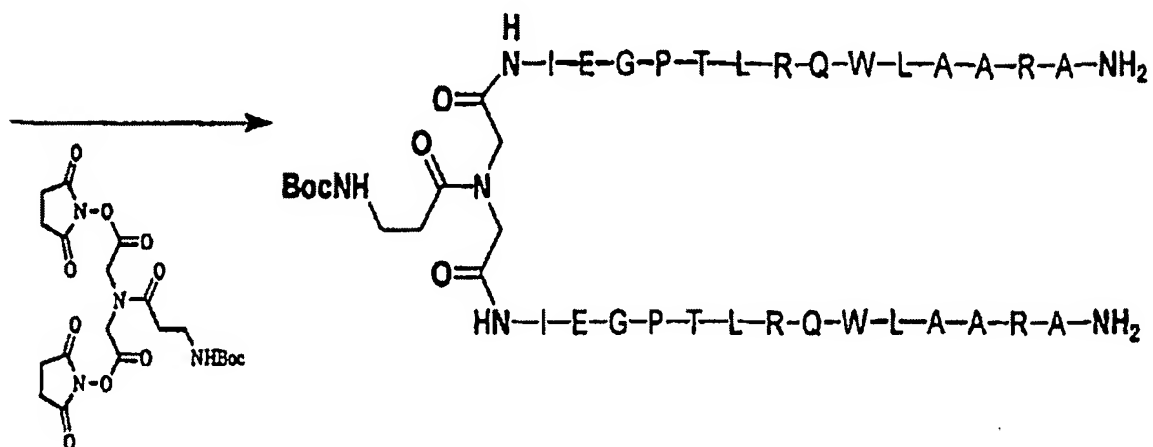
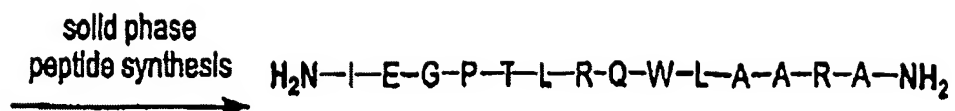


FIG. 15D

A trifunctional molecule having the structure

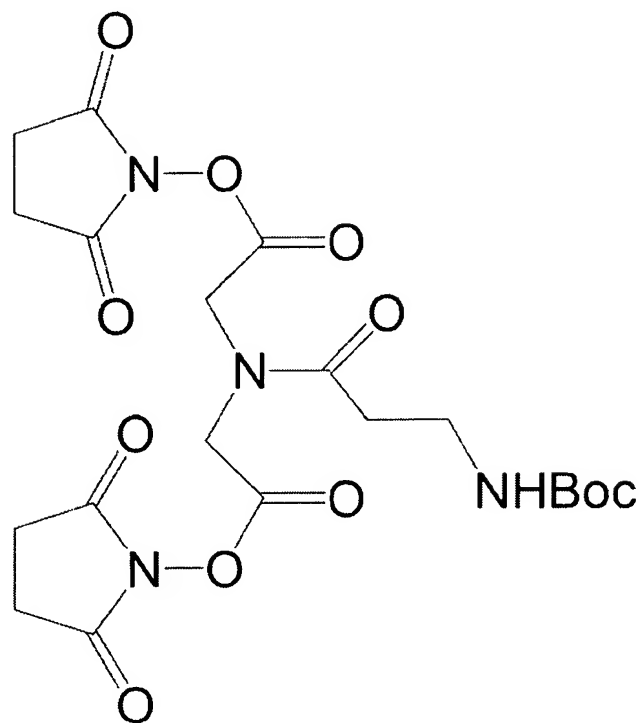


FIG. 16A

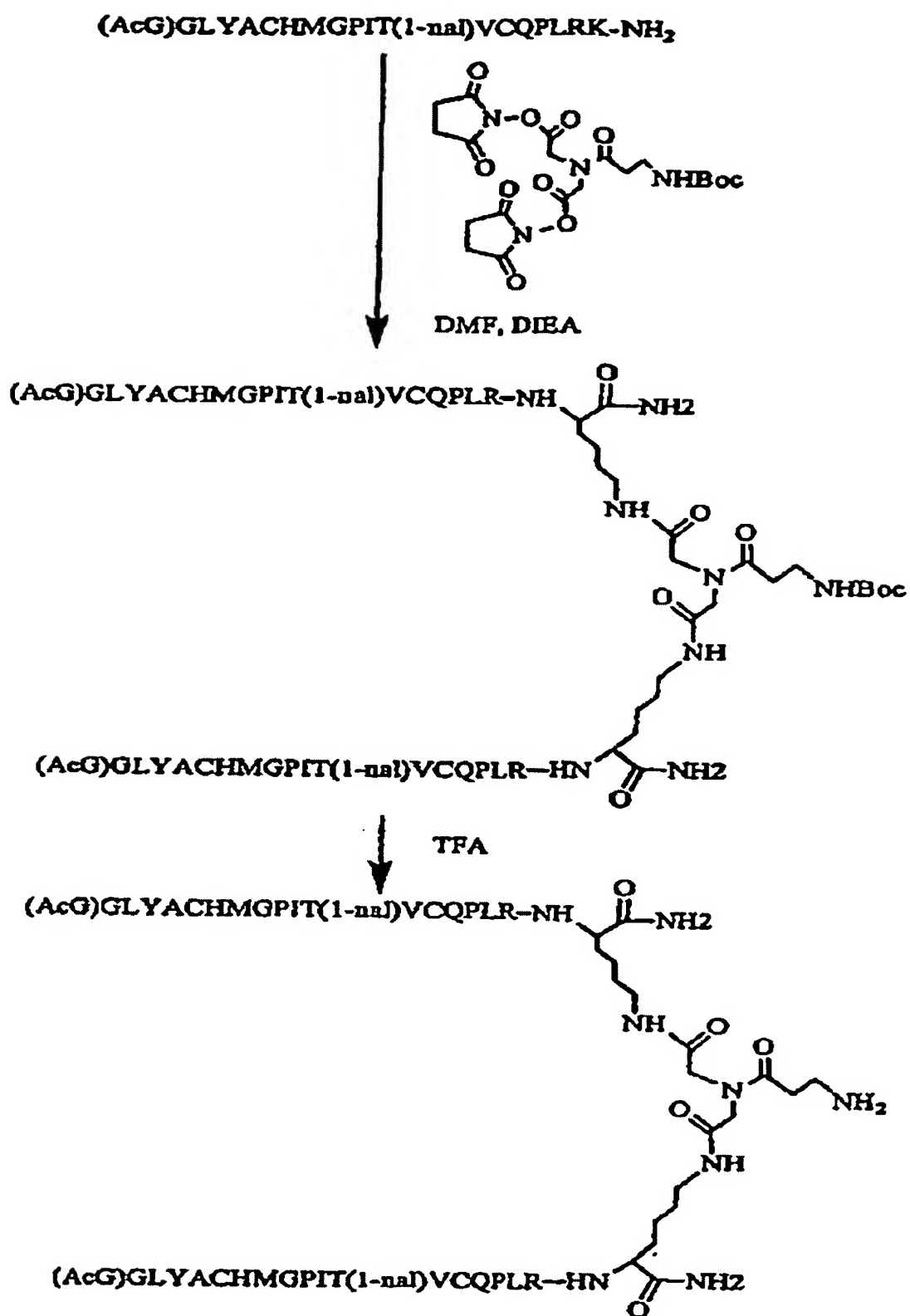


FIG. 16B

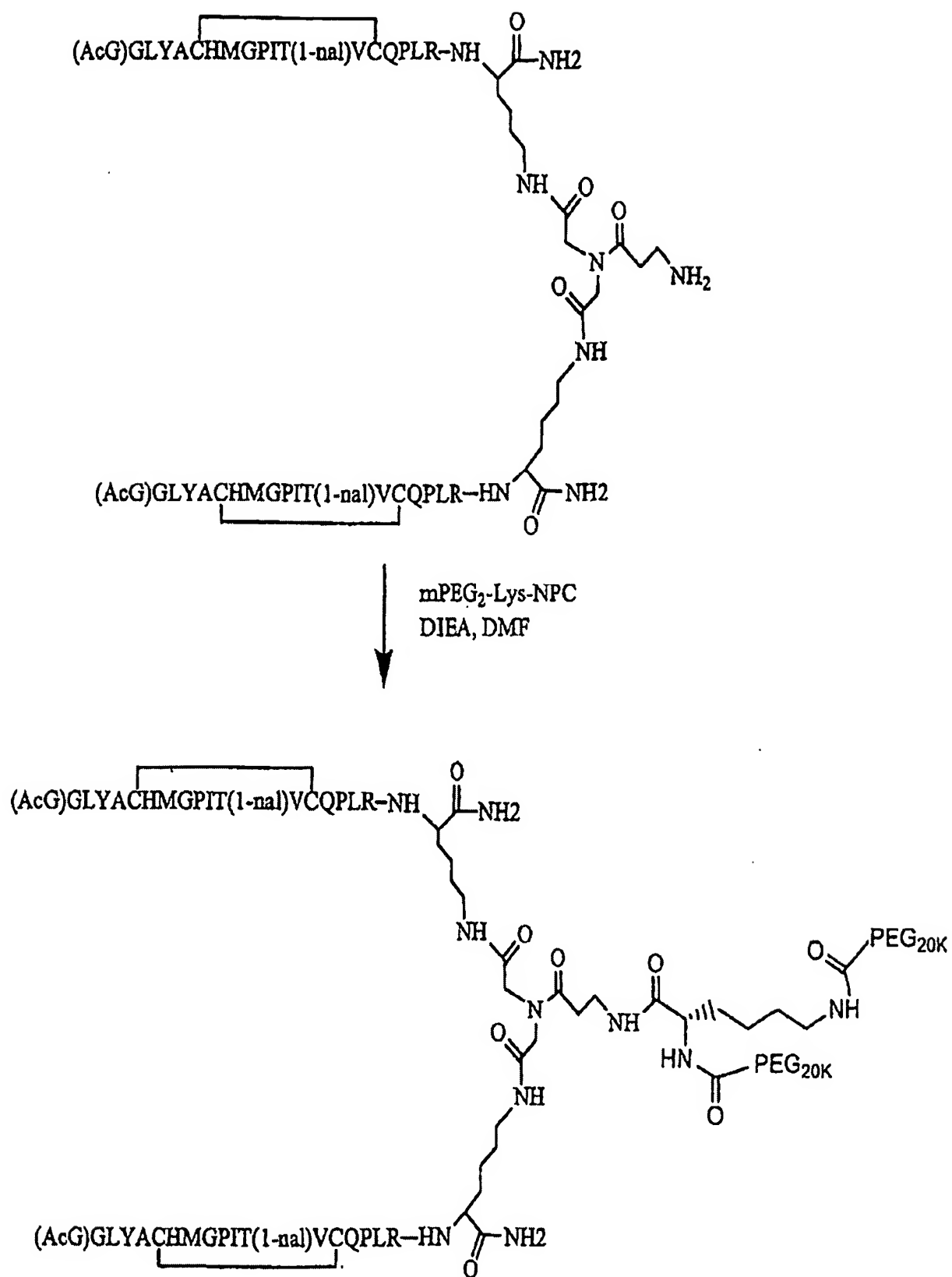


FIG. 16C

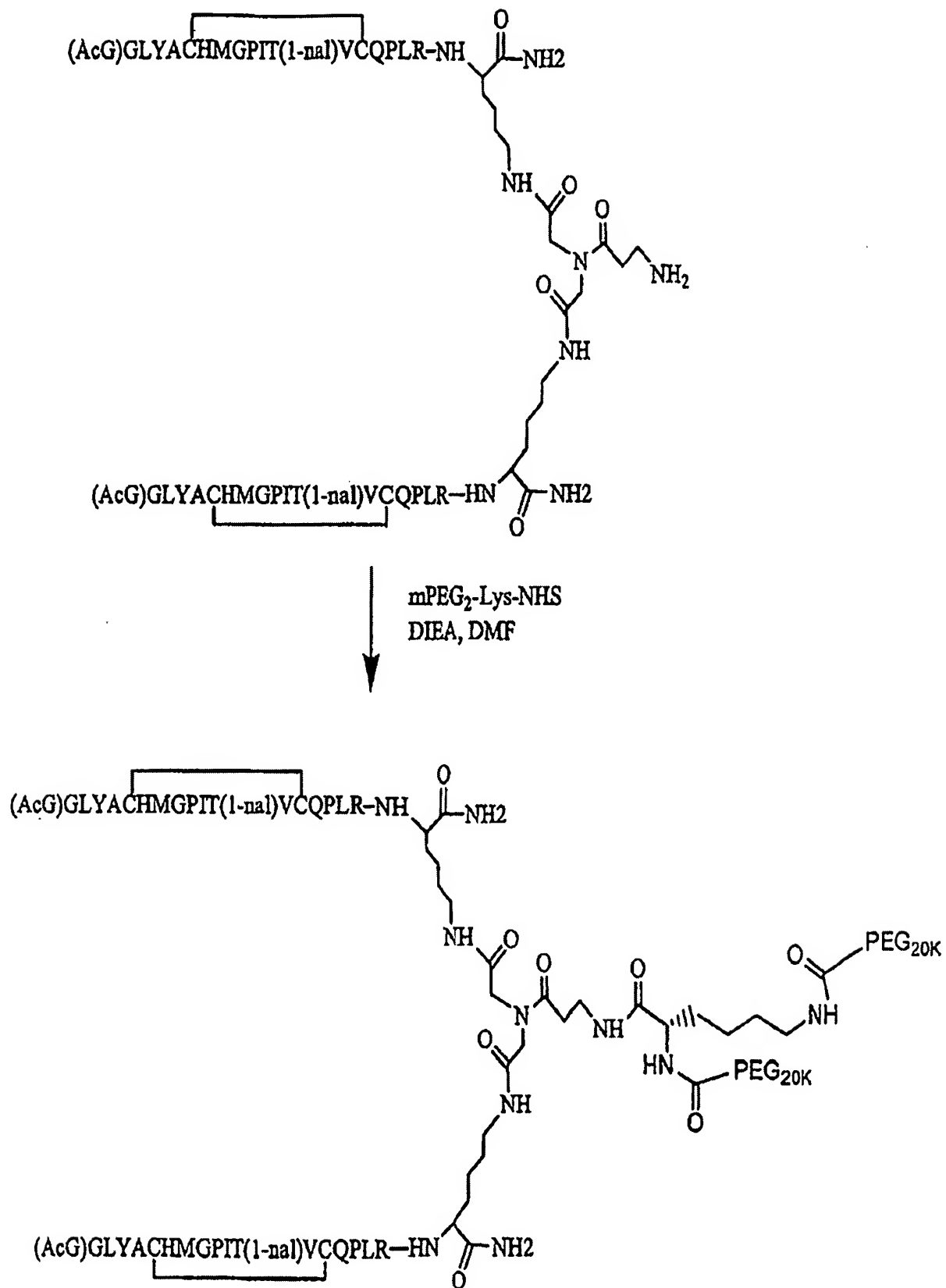


FIG. 16D